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EXAMINER

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ART UNIT PAPER NUMBER

1634

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/803,713	Applicant(s) MARQUESS ET AL.	
	Examiner Stephen Kapushoc	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-22 is/are rejected.
- 7) ☒ Claim(s) 1, 11, 12, 19 is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 18 March 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|-----------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____. |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Claims 1-22 are pending and examined on the merits.

Priority

1. The specification (page 1) of the instant application claims benefit as a CIP of US application 10/770,307 (filed 2/2/04) which claims benefit of the filing dates of US provisional applications 60/466,523 (4/29/03), 60/509,775 (10/8/03), and 60/456,489 (3/21/03). It is believed that the claim to benefit to US provisional application 60/509,775 is a typographical error, and the proper claim should be made to application 60/509,755 (filed 10/8/2003). The application also claims priority to Canadian Application 2/422,437 (filed 3/18/2003); it is noted that the Declaration associated with the instant application incorrectly identifies the filing date of Canadian Application 2/422,437 as 3/18/2002.

Acknowledgment is made of applicant's claim for foreign priority based on Canadian Application 2/422,437. It is noted, however, that applicant has not filed a certified copy of the Canadian application as required by 35 U.S.C. 119(b).

The instant claims encompass methods for selecting animal having a greater feed conversion efficiency. However basis for such claims is not found in 60/456,489 or Canadian Application 2/422,437. Thus claims drawn to methods for selecting animal having a greater feed conversion efficiency are not given the benefit of the filing dates of 60/456,489 or Canadian Application 2/422,437.

Information Disclosure Statement

2. The listing of references in the specification is not a proper information disclosure statement; see for example the citation of references on page 2 of the instant specification. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specification

3. The disclosure is objected to because of the following informalities:

The specification makes reference to methods 'using primers having SEQ ID NO: 2 and 3' (see for example page 52). However, in the sequence listing for the instant application, SEQ ID NO: 2 does not appear to be an oligonucleotide primer suitable for use in PCR, and SEQ ID NO: 3 is an amino acid sequence. Applicant is encouraged to thoroughly check the specification to ensure that the various SEQ ID NOs throughout the specification are used as intended.

Appropriate correction is required.

Oath/Declaration

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4. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

It does not identify the foreign application for patent or inventor's certificate on which priority is claimed pursuant to 37 CFR 1.55, and any foreign application having a filing date before that of the application on which priority is claimed, by specifying the application number, country, day, month and year of its filing.

In the instant case the oath indicates a filing date of Canadian Application 2/422,437 as 3/18/2002, whereas the application appears to be filed 3/18/2003.

Additionally, the Oath/Declaration makes reference to US provisional application 60/509,775 where likely 60/509,755 is intended.

Claim Objections

5. Claim 1 is objected to because of the following informalities:

The first step of the method is identified with the letter (c). This should be edited such that the step is identified with the letter (a) if applicant intends this to be the first stated method step.

6. Claim 12 is objected to because of the following informalities:

The claim recites the phrase 'compared to general population of animals' where perhaps 'compared to a general population of animals' is intended.

7. Claims 11 and 19 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim.

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Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

8. In the instant case claim 11 is drawn to a method comprising selecting animals with either a TT or TC genotype; however claim 10 (from which claim 11 depends) is drawn to a method comprising selecting animals that possess the T-containing allele of the ob gene (as recited in the base claim 8). Animals that 'possess the T-containing allele of the ob gene' are animals with the TT or CT genotypes. It is thus unclear how claim 11 further limits the claim from which it depends.

In the instant case claim 19 is drawn to a method comprising selecting animals with either a TT or TC genotype; however claim 18 (from which claim 19 depends) is drawn to a method comprising selecting animals that possess the T-containing allele of the ob gene (as recited in the base claim 16). Animals that 'possess the T-containing allele of the ob gene' are animals with the TT or CT genotypes. It is thus unclear how claim 19 further limits the claim from which it depends.

Appropriate corrections are required.

Claim Rejections - 35 USC § 112 2nd - Indefiniteness

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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10. Claim 1-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-7 are unclear over recitation of the phrase 'amplifying a region of the ob gene polymorphism' in claim 1 because it is unclear if Applicant intends for the amplified sequence to encompass and included the polymorphic position, or to be in some other way associated with the polymorphic position.

Claims 1-7 are unclear over recitation of the phrase 'the amplified ob gene polymorphism sequences' in claim 1 because there is no antecedent basis for any amplified ob gene polymorphism sequences in the claim.

Claims 1-7 are unclear over recitation of the phrase 'based on the presence of a particular ob gene polymorphism' in claim 1 because it is unclear if applicant intends for the identification to be based on the finding the a particular position within the ob gene is polymorphic, or for the identification to be based on the finding of a particular nucleotide content at a specific polymorphic position in the ob gene.

Claims 1-7 are unclear over recitation of the phrase 'selecting the type of livestock animal' in claim 1 because it is unclear if applicant intends for the selection of different type of livestock, for example selecting a pig versus a cow versus a goat, or an animal with a particular trait.

Claim 3 is unclear because while the claim further limits claim 1 by require the selecting of animals having greater feed conversion efficiency, the preamble of claim 1

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indicates a method of identifying animals having greater milk productivity, and step (b) of claim 1 is the identification of animals having greater milk productivity based on the presence of a polymorphism. It is thus unclear how the purpose of the claim, as stated in the preamble, is accomplished by the method step of the claim.

Claims 8-11, 20, 21, and 22 are unclear because while the preamble of the claim states that the claim is drawn to a method of increasing milk production in a selected group of livestock, there is no method step in which the milk production of any group is actually increased. It is thus unclear how the purpose of the claim, as stated in the preamble, is accomplished by the method steps of the claim.

Claims 12, 13, 20, 21, and 22 are unclear because while the preamble of the claim states that the claim is drawn to a method of identifying those animals having increased milk productivity, there is no method step in which any animal is actually identified according to its milk productivity. It is thus unclear how the purpose of the claim, as stated in the preamble, is accomplished by the method steps of the claim.

Claims 14, 15, 20, 21, and 22 are unclear because while the preamble of the claim states that the claim is drawn to a method of breeding livestock animals to increase milk production in the offspring, there is no method step in which any animal is actually bred or the milk production in any offspring is increased. It is thus unclear how the purpose of the claim, as stated in the preamble, is accomplished by the method steps of the claim.

Claims 16-22 are unclear because while the preamble of the claim states that the claim is drawn to a method of increasing milk production in a selected group of livestock

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animals, there is no method step in milk production of any group is actually increased.

It is thus unclear how the purpose of the claim, as stated in the preamble, is accomplished by the method steps of the claim.

Claims 2, 3, 10, 11, 13, 18 and 19 are unclear over the recitation of the phrase 'with respect to' in reference to an allele of the ob gene. For example, claim 2 recites 'a TT animal homozygous with respect to the T-allele of the ob gene', where it is unclear if applicant intends to claim an animal with particular nucleotide content at a specific polymorphic position in a particular gene, or some other content at another position in some way related the polymorphic position.

Claim Rejections - 35 USC § 112 1st - Description

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 1-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is referred to the revised interim guidelines on written description published January 5, 2001 in the Federal Register, Volume 66, Number 5, page 1099-111 (also available at www.uspto.gov).

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The claims of the instant application are drawn to methods for the identification and selection of animals with particular phenotypes based on the analysis of nucleic acid sequences. The claims are broadly drawn to the detection and selection of animals with the T-allele or the C-allele of the ob gene. While claim 1 requires the amplification of a region of the ob gene with the primer pair of SEQ ID NO: 4 and 5 and hybridization with probes consisting essentially of SEQ ID NO: 6 and 7, because it is unclear how SEQ ID NOs: 4-7 are related to the sequences of the ob gene, and the specification provides no examples of a method for detecting any ob gene polymorphisms using SEQ ID NOs: 4-7, it is not clear how these sequences address the description of the T-allele or the C-allele of the ob gene. Claims 1, 2, 3, 4, 8-19 encompass the analysis of any animal. Claims 5 and 20 encompass the analysis of any bovine, ovine, avian, or swine. Claims 6 and 21 require the analysis of bovines, and claims 7 and 22 require that the analyzed bovine is a dairy cattle.

The specification further provides the sequence of a portion of the ob gene from bovine as SEQ ID NO: 1 and 2, where SEQ ID NO: 1 has a T at position 189 and SEQ ID NO: 2 has a C at position 189. The specification asserts that any ob gene corresponding to any animal of interest can be used to identify the polymorphism(s) of interest (p.32), and provides GenBank accession numbers for several sequences corresponding to sequences obtained from bovine, ovine, swine, and avian organisms (p.34). However, while the specification provides reference to GenBank entries, neither the specification nor the sequence listing contain any information pertaining to the gene sequence in other organisms, or polymorphic position with any sequence known as a T-

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allele or a C-allele. Reliance upon GenBank records does not provide an adequate written description for the claimed invention, as the content in a GenBank record can change over time as the records can be updated as time passes. In this case a potential update to the any cited GenBank record may result in a change in the nucleotide sequence associated with that GenBank accession number. Thus the reliance of an external GenBank sequence for a numbering scheme is similar to the recitation of a trademark, in that the GenBank accession number does not represent a fixed disclosure of a sequence, but instead refers to a record that is constantly able to be updated and modified. Similarly, reference to a nucleic acid sequence simply by a gene identifier such as 'ob' does not provide any structural limitations to the sequence analyzed in the claimed methods. The claims thus encompass a wide variety of distinct nucleic acid sequences which are broadly addressed as T-allele or C-allele of the ob gene.

In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. The instant specification provides only the sequences of SEQ ID NOs: 1 and 2 as the sequences of portions of the bovine ob gene containing a T or a C at position 189, respectively. The specification also provides the nucleotide sequences of SEQ ID NO: 4, 5, 6, and 7, asserted by the specification to be primers and probes specific for the ob gene (p.37), however it is unclear how these sequences are related to the sequences provided as SEQ ID NO: 1 and 2, or any other ob gene sequence. The specification provides no other ob gene sequences, nor any

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other polymorphic variants of any ob gene.

Next, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (e.g. other than nucleotide sequence or position within a particular gene), specific features and functional attributes that would distinguish different members of the claimed genus. In the instant case, while the specification asserts that any ob gene from any animal can be used (p.32), there is no guidance as to identify a T-allele or C-allele of an ob gene with the required functionality (i.e. indicative of a milk production or feed conversion traits), and in fact the specification provides no guidance as to how one may *a priori* identify either an ob gene or a polymorphism in an ob gene that is a T-allele or C-allele indicative of a phenotype.

Applicants' attention is directed to the decision in *In re Shokal*, 113 USPQ 283 (CCPA 1957) wherein is stated:

It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. *In re Soll*, 25 C.C.P.A. (Patents) 1309, 97 F.2d 623, 38 USPQ 189; *In re Wahlforss et al.*, 28 C.C.P.A. (Patents) 867, 117 F.2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, or perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary.

In the instant application, because the only structural information provided regarding polymorphic nucleic acid sequence variants related to milk productivity and feed conversion are the sequences of SEQ ID NO: 1 and 2, one of skill in the art cannot envision the detailed chemical structure of the nucleic acids encompassed by the claimed methods (i.e. a T-allele of an ob gene in any organism), regardless of the

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complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that such nucleic acids are part of the invention and reference to a potential method for identification. The particular nucleic acids are themselves required.

In conclusion, the limited information provided regarding the nucleic acids of the claimed methods is not deemed sufficient to reasonably convey to one skilled in the art that Applicant is in possession of a method for identifying animals with particular phenotypic traits based on the determination of gene polymorphisms or T-alleles and C-alleles of an ob gene, at the time the application was filed.

Thus, having considered the breadth of the claims and the provisions of the specification, it is concluded that the specification does not provide adequate written description for the claims.

Claim Rejections - 35 USC § 112 1st – Scope of Enablement

13. Claims 1-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A method for identifying a bovine dairy cattle having greater milk productivity comprising detecting at least one copy of SEQ ID NO: 1 in said bovine dairy cattle, and identifying the bovine dairy cattle having at least one copy of SEQ ID NO: 1 as an animal having greater milk productivity as compared to a bovine dairy cattle having two copies of SEQ ID NO: 2, wherein the greater milk productivity is an increased milk production during the first 100 days of lactation,

does not reasonably provide enablement for the detection of any other measure of milk productivity, or feed conversion efficiency, by the detection of any other particular nucleotide content or the analysis of any animals other than bovine dairy cattle. The

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specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Nature of the invention and breadth of the claims

The claims are drawn to methods for the identification of animals with particular phenotypic traits based on the determination of nucleotide content at polymorphic positions in the ob (leptin) gene.

The claims encompass any measure of increased milk productivity.

Claim 3 encompasses any measure of feed conversion efficiency.

Claims 1-3 and 4-22 encompass the detection of any T-allele or C-allele of any ob gene.

Claim 4 encompasses the detection of any ob gene polymorphism that is a C to T transition that results in Arg25Cys.

Claims 1, 2, 3, 4, 8-19 encompass the analysis of any animal. Claims 5 and 20 encompass the analysis of any bovine, ovine, avian, or swine. Claims 6 and 21 require the analysis of bovines, and claims 7 and 22 require that the analyzed bovine is a dairy cattle.

The nature of the claims requires knowledge of the association of particular ob gene variants in different animals and phenotypes related to milk production and feed conversion efficiency.

Direction provided by the specification and working example

The instant specification provides any analysis of the detection of SEQ ID NO: 1 and 2 (where SEQ ID NO: 1 has a T at position 189 and SEQ ID NO: 2 has a C at position 189) in bovine dairy cattle and the association of particular phenotypic traits in animals with either 1 or two copies of SEQ ID NO: 1 as compared to animals with two copies of SEQ ID NO: 2. The specification teaches (Table 3, p.70) that animals with either one or two copies of SEQ ID NO: 1 (the T containing allele) have a statistically significant increase in the amount of milk produced (as measured in kilograms/day) during the first 100 days of lactation compared to animals having two copies of SEQ ID NO: 2 (the C containing allele).

The instant specification teaches that analysis of ob gene alleles was by a previously disclosed PCR-RFLP method (Example 1 - p.68). The specification does not provide any example in which particular polymorphisms of the ob gene are determined using SEQ ID NOs: 4, 5, 6, and 7.

The instant specification does not provide any analysis of any nucleotide sequences other than SEQ ID NOs: 1 and 2, nor any polymorphic positions other than position 189 of SEQ ID NOs: 1 and 2 where position 189 is either a T or a C.

The specification does not provide any analysis of any other animals other than bovine dairy cattle.

State of the art, level of skill in the art, and level of unpredictability

While the state of the art and level of skill in the art with regard to the detection of any particular nucleic acid sequence, or the detection of a polymorphic variant in a

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particular sequence is high, the level of unpredictability with regard to associating the presence of a nucleic acid sequence or any particular polymorphic variation, to any particular phenotype is even higher. The unpredictability is demonstrated by the prior art, the post filing art, and the instant specification.

Because the claims encompass the detection of polymorphisms in the ob gene using PCR amplification primers of SEQ ID NO: 4 and 5 and hybridization probes consisting essentially of SEQ ID NO: 6 and 7 it is relevant to point out that while the specification asserts that such nucleic acids (page 37-38) can be used for the analysis of the ob gene polymorphisms of SEQ ID NO: 1 and 2, the specification does provide any example in which the aforementioned primers and probes are actually used in ob gene analysis. A search of the nucleotide sequences of SEQ ID NO: 4, 5, 6, and 7 does not indicate that these sequences are in any way related to the ob gene, or the particular T to C polymorphism of SEQ ID NO: 1 and 2. It is thus entirely unpredictable as to how one might use such sequences in an analysis of any ob gene.

Because the claims encompass any measure of milk productivity it is relevant to point out that while the instant specification teaches that animals with one or two copies of the T-containing allele (SEQ ID NO: 1) have a statistically significant increase in the number of kilograms of milk produced per day during the first 100 days of lactation as compared to animals having two copies of the C-containing allele (SEQ ID NO: 2), there is not a statistically significant increase during the entire lactation, or during the time period of 200 days after the start of lactation (Table 3). It is thus

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unpredictable as to how one might identify an animal with greater milk productivity during an entire lactation by an analysis of ob gene polymorphisms.

Because the claims encompass a C to T transition that results in Arg25Cys it is relevant to point out that while the specification teaches a particular polymorphism (T to C at position 189 in SEQ ID NO: 1 to SEQ ID NO: 2) that causes an Arg to Cys change in an amino acid sequence encoded by SEQ ID NO: 1 and 2, the specification teaches, for example, that the bovine amino acid sequence can be the sequence from GenBank AAE82807 (p.33 of the specification). However, a sequence corresponding to GenBank AAE82807 contains neither a Cys or an Arg at position 25. It is thus entirely unpredictable as to whether or not a polymorphism that can be identified as 'a C to T transition that results in Arg25Cys' would in fact be indicative of a particular phenotype in the same was as the particular polymorphisms actually analyzed in the example of the instant specification.

Because the claims are drawn to the detection of the T-allele and C-allele of the ob gene, it is relevant to point out that while the specification teaches a particular T to C polymorphism (at position 189 in SEQ ID NO: 1 to SEQ ID NO: 2), there are other polymorphisms in the bovine ob gene, distinct from the polymorphism of the instant application, that can be considered T-alleles and C-alleles of the ob gene. For example, the post-filing art of Madeja et al (2004) teaches that there is an HphI polymorphism (a C/T substitution resulting in a change from valine to alanine) in exon 3 of the bovine gene (p.3925, right col., Ins.13-14), and addresses the genotype of animals as CC, CT, and TT in reference to this polymorphism (Table 2; p.3926, left col). It is thus

unpredictable as to how the detection of an allele broadly described as, for example 'the T-containing allele of the ob gene' would be used to identify an animal having any particular phenotypic trait.

Because the claims encompass methods wherein 'TT animals homozygous with respect to the T-allele of the ob gene have a greater milk productivity than CT animals heterozygous with respect to the T-allele' (claim 13) it is relevant to point out that the data presented in Example 1 (Table 3) compares only the TT genotype and TC genotype with the CC genotype, and there is in fact no indication of a statistically significant difference between milk production in TT animals as compared to CT animals.

The claims encompass the identification and selection of animals having a greater feed conversion efficiency, which could encompass the efficiency with which any animal converts feed to milk, fat, muscle, or total body weight. The instant specification provides Example 3 (pages 73-78), which is a proposed analysis of leptin genotype associated with milk production and energy balance, but does not provide any results regarding any statistically significant association between genotype and feed conversion. Additionally, Example 4 (pages 78-82) is a study of the relationship between leptin genotype, milk production, milk compositions, and dry matter intake. However, Example 4 does not indicate whether or not there is any statistically significant correlation between any particular genotype and feed conversion efficiency as determined by, for instance, pounds of dry matter per kilograms of milk produced per day. Similarly, provisional application 60/509,755 provides no statistically significant

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correlation between leptin genotype and dry matter per pound gained in a study of 8 cattle (2 TT, 3 CT, and 3 CC), and provisional application 60/466,523 does not teach a study in which feed conversion is analyzed in a controlled manner (e.g. the amount of dry matter consumed by any particular animal is recorded and related to genotype and carcass grade). Thus while the specification does not provide any statistically significant correlation between genotype and any measure of feed conversion efficiency, the prior art of Thisted (1998) provides guidance as to what is required to indicate that an association is statistically significant (Thisted teaches that it has become scientific convention to say that a P-value of 0.05 is considered significant (p.5 - What does it mean to be 'statistically significant'), and that values above the conventional reference point of 0.05 would not be considered strong enough for the basis of a conclusion). It is thus unpredictable as to whether or not one can reliably identify an animal with greater feed conversion efficiency based on ob gene polymorphism detection.

While the claims encompass the analysis of any ob gene from any animal, it is relevant to point out the unpredictability with regard to analyzing genetic elements among different organisms. While it is generally held true that structure correlates with function, Bork et al (1993) teaches an analysis of sugar kinases, and indicates that very distinct proteins (with different three-dimensional structures and strikingly different sequence patterns) can catalyze chemically equivalent reactions of similar or identical substrates (p.31 - Abstract). Additionally, sequences that appear quite similar may in fact have very different functionalities. Such a possibility is exemplified by Juppner

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(1995), which teaches that despite significant structural conservation, rat, opossum, and human PTH/PTHrP receptor homologs display distinct functional characteristics (Abstract; pp.39S-40S). Thus it is highly unpredictable as to how one would extrapolate methods or results regarding association of any particular specific leptin genotype consisting of SEQ ID NO: 1 or 2 and associated with milk productivity in bovine dairy cattle with any association in any other different animal.

Quantity of experimentation required

A large and prohibitive amount of experimentation would have to be performed in order to make and use the claimed invention in the full scope of the claims. Such experimentation would require determining that particular ob polymorphisms are associated in a significant fashion with any measure of milk productivity (such as milk production over the entire lactation). Given the breadth of the claim language regarding the determined polymorphism (e.g. C-allele of the ob gene), one would also be required to analyze the nucleotide content at a large number of positions within any ob gene sequence to determine associations with milk production or feed conversion efficiency. One would also have to determine how the use of primers and probes of SEQ ID NO: 4, 5, 6, and 7 would provide information regarding any ob gene polymorphisms related to milk production or feed conversion. Such experimentation would also include examining ob gene polymorphisms from any organism and determining any association with any measure of milk production and feed conversion efficiency. The required experimentation would involve the analysis of an enormous number of polymorphic sequences, and large case:control studies in multiple populations.

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Conclusion

Taking into consideration the factors outlined above, including the nature of the invention and breadth of the claims, the state of the art, the level of skill in the art and its high level of unpredictability, the lack of guidance by the applicant and the specific working example, it is the conclusion that an undue amount of experimentation would be required to make and use the claimed invention in the full scope of the claims.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 8-13 and 20-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Konfortov et al (1999) as evidenced by GenBank GI: 4468136 (1999).

Konfortov et al teaches an analysis of polymorphic positions of the bovine ob (leptin) gene. The analysis includes the polymorphic 305 C/T position (Table 2) which is equivalent to the polymorphism of position 189 of SEQ ID NO: 1 and 2 of the instant application, as evidenced by GenBank GI: 4468136.

Regarding claim 8, Konfortov et al teaches determining the genotype of animals within the leptin gene, which is the ob gene (p.1142 – Materials and methods). The reference teaches determining the genotype at the 305 C/T polymorphic position in the leptin gene, which is inherently associated with milk production, relevant to step (a).

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The reference teaches the grouping of genotyped animals in Figure 2, where CC animals are in a group with green squares in column four, TT animals are grouped with red squares in column four, and CT animals are grouped with blue squares in column four. Thus animals with T-containing alleles are grouped with red and blue (not green) squares in column four.

Regarding claim 9, the TT and CT animals grouped with red and blue (not green) squares in column four (Fig 2) have genotypes that are inherently associated with increased milk production during the first 100 days of lactation.

Regarding claim 10, Konfortov et al teaches determining the genotype of animals within the leptin gene, which is the ob gene (p.1142 – Materials and methods). The reference teaches determining the genotype at the 305 C/T polymorphic position in the leptin gene including TT, CT, and CC genotypes.

Regarding claim 11, Konfortov et al teaches the selection of animals with T-containing alleles are grouped with blue and red (not green) squares in column four.

Regarding claim 12, Konfortov et al teaches the identification of animals with T-containing alleles of the ob gene, where the allele possesses a T at position 305 of the leptin gene (as indicated in GenBank GI: 4468136), which is an allele that is inherently associated with increased milk production.

Regarding claim 13, Konfortov et al teaches group of animals that are homozygous TT for the ob gene genotype, as well as animals that are CT heterozygous for the ob gene genotype.

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Regarding claims 20, 21, and 22, the reference teaches the analysis of several breed of cows, including bovines that are dairy breeds, such as Jersey (Table 1).

It is noted that this rejection of claims under 35 USC 102 cites multiple references. However, the additional reference (GenBank GI: 4468136) is cited as it provides evidence of the inherent characteristics of the method of Konfortov et al, specifically that the methods taught by Konfortov et al comprise analysis of a polymorphic variant of the ob (leptin) gene inherently associated with milk productivity (see MPEP 2131.01).

Conclusion

16. No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Kapushoc whose telephone number is 571-272-3312. The examiner can normally be reached on Monday through Friday, from 8am until 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Art Unit 1634


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